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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,109	06/22/2006	Kenichiro Kosai	55801-003US1	8348

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/584,109	KOSAI ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,11,14,16,17,24 and 29-42* is/are pending in the application.

4a) Of the above claim(s) *1,3,4,11,29,30 and 40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 16-17, 24 and 31-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/19/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of an adenovirus as a species of an expression vector in the reply filed on 12/16/09 is acknowledged.

Amended claims 1, 3-4, 11, 14, 16-17, 24 and new claims 29-42 are pending in the present application.

Claims 1, 3-4 11, 29-30 and 40-42 were withdrawn from further consideration because they are directed to non-elected species.

Accordingly, claims 14, 16-17, 24 and 31-39 are examined on the merits herein with the above elected species.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, for lack of Written Description was withdrawn in light of Applicant's amendment, particularly with the new limitation "an effective amount of an expression vector containing a sequence encoding a CD9 protein".

The rejection under 35 U.S.C. 102(b) as being anticipated by Miyake et al (Oncogene 19:5221-5226, 2000) was withdrawn in light of Applicant's amendment, particularly amended independent claim 1 no longer encompasses the elected species and independent new claim 31 with the new limitation "the CD9 gene is promotered by a Rous sarcoma virus (RSV) promoter".

The rejection under 35 U.S.C. 102(a) as being anticipated by Ushikoshi et al (Circulation, Supplement III, 110, page 8, 2004) was withdrawn in light of Applicant's

submission of a copy of the English translation of the foreign priority document JP 2003-432279, filed on 12/26/2003 in Exhibit C along with a Verification of Translation in Exhibit D.

Claim Objections

Claim 31 is objected to the phrase "expression of the CD9 gene is promotered by a Rous sarcoma virus (RSV) promoter" because the term "promoter" is commonly used as a noun. The examiner suggests replacing the above phrase with - - expression of the CD9 gene is under the control of a Rous sarcoma virus (RSV) promoter - -.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 14, 16-17, 24 and 35-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is new ground of rejection necessitated by Applicant's amendment.***

Amended independent claims 14, 16-17, 24 and 35-39 recite the new limitation "**or via a coronary artery supplying a cardiac muscle in the heart of a subject in**

need thereof". The specification as originally filed does not provide a written support for this specific embodiment in the methods as now claimed. In the amendment filed on 8/11/09 (page 6), Applicants cited lines 22-25 at page 6 as alleged supports for the above limitation. Applicants further argue that as commonly known, a balloon catheter is positioned by a cardiologist into a coronary artery during cardiac catheterization; and referred the examiner to the definition of "a balloon catheter" from Wikipedia (Exhibit A). However, lines 22-25 at page 6 simply state "The administration form of the drug of the present invention is not particularly restricted, and for example, injection, catheter, balloon catheter and the like can be adopted." It is apparent that this statement does not support in any shape or form the specific concept of administering the drug of the present invention via a coronary artery supplying a cardiac muscle in the heart of a subject. Please note that a balloon catheter can be inserted into an artery or a vein in the arm or leg of a patient via cardiac catheterization as well to being advanced to chambers of the heart, and not necessarily to be only to the coronary arteries as evidenced by the definition of the term "cardiac catheterization" from the American Heart Association. Additionally, Exhibit A also discloses that a balloon catheter is commonly used via cardiac catheterization.

Therefore, given the lack of sufficient guidance provided by the originally filed specification, it would appear that Applicants did not contemplate or have possession of invention as now claimed at the time the application was filed.

Claim Rejections - 35 USC § 112 - Enablement

Amended claims 14, 16-17, 24 and 35-39 are still rejected in part under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for suppressing cardiac hypertrophy or cardiac tachycardia in a subject having a heart disease, said method comprises administering directly to a cardiac muscle in the heart of said subject an expression vector comprising a sequence encoding a CD9 protein, wherein the heart disease is characterized by myocardial infarction, hypertrophy, arrhythmia or tachycardia, and wherein cardiac hypertrophy or cardiac tachycardia is suppressed in said subject;

does not reasonably provide enablement for a method for treating a heart disease in any other subject as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reason already set forth in the Office action mailed on 3/11/09 (pages 5-10).

Response to Arguments

It is noted that Applicants' arguments in the Amendment filed on 8/11/09 (pages 8-10) have been fully considered and they overcame most issues that are set forth in the Office action dated 3/11/09. However; they did not address the specific issue of the limitation "a subject in need thereof".

Firstly, please note that currently amended claims still encompass a method for treating a heart disease comprising expressing a CD9 gene in the heart of any subject in need thereof, not necessarily limited to a subject already has symptoms of a heart

disease or having a heart disease. As already noted in the previous office action, the instant specification fails to provide sufficient guidance for a skilled artisan on how to attain any prophylactic effect (e.g., preventing the onset of the recited heart disease for any period of time such as 1 week, 1 month, 1 years to several years in a subject in need thereof) within a broad "treatment" scope for a subject that does not even have any symptom of a heart disease, as encompassed by the presently claimed invention. Since the prior art at the effective filing date of the present application does not provide such guidance on this issue, it is incumbent upon the present application to do so. Therefore, at least in light of the state of the gene therapy art and the state of the art on treating a heart disease with CD9/DRAP27, coupled with the lack of sufficient guidance provided by the instant specification it would have required undue experimentation for a skilled artisan to make and use the treatment method as broadly claimed.

Secondly, with respect to the new limitation "via a coronary artery supplying a cardiac muscle in the heart of a subject in need thereof" the instant specification does not have a written support for this new limitation. Please refer to the above New Matter rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

New claims 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyake et al (Oncogene 19:5221-5226, 2000) in view of Li et al. (US 6,638,502).

This is a new ground of rejection necessitated by Applicant's amendment.

The claims are directed to a drug for treating a heart disease characterized by cardiac hypertophy or tachycardia, comprising a viral expression vector containing a CD9 gene as the active ingredient and a pharmaceutically acceptable auxiliary or carrier, wherein the viral expression vector is adenovirus; and wherein expression of the CD9 gene is promotered by a Rous sarcoma virus promoter. *It is noted that for a composition claim, its intended use is not given any patentable weight in light of the prior art.*

Miyake et al already disclose a composition comprising a replication-deficient adenovirus encoding MRP-1/CD9 cDNA operably linked to a human CMV gene promoter, in a virus dialysis buffer or balanced salt solution (a pharmaceutically acceptable auxiliary or carrier) for intratumoral injection; and the composition results in a

73.7% reduction in the number of pulmonary metastasis of mice and a significantly longer median survival time of mice treated with rAd-MRP-1/CD9 relative to mice treated with the rAd-β-gal vector (see at least the abstract; page 5225, col. 1, top of second paragraph and col. 2, section titled "MRP-1/CD9 gene therapy"). Miyake et al further stated "Considering that despite improved chemotherapeutic and radio-therapeutic procedures, no therapeutic modalities have been shown to be effective in preventing metastases or improving the 5-year survival rate of patients with distant metastasis, prevention of metastases using MRP-1/CD9 gene therapy might be one of the most important modalities" (page 5224, col. 2, last sentence of first paragraph).

Miyake et al do not teach specifically the use of a replication-deficient adenovirus encoding MRP-1/CD9 cDNA under the control of a Rous sarcoma virus promoter.

However, at the effective filing date of the present application (12/26/2003) Li et al already taught at least the use of a recombinant replication defective adenovirus encoding an anti-angiogenic factor to inhibit tumor growth and metastasis, wherein the expression of an anti-angiogenic factor is under the control of a promoter such as CMV promoter, SV40 early promoter region, Rous sarcoma virus promoter and others (see at least Summary of the invention; particularly col. 14, lines 37-48; col. 15, lines 4-6).

It would have been obvious for an ordinary skilled artisan to modify the composition of Miyake et al by also expressing MRP-1/CD9 cDNA under the control of a Rous Sarcoma virus promoter for treating tumor metastasis in light of the teachings of Li et al as discussed above.

An ordinary skilled artisan would have been motivated to carry out the above modification because at least Li et al already taught that CMV promoter and RSV promoter have been successfully used to express a therapeutic gene in a recombinant replication defective adenovirus for inhibiting tumor growth and metastasis.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Miyake et al and Li et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art. The modified composition resulting from the combined teachings of Miyatake et al and Li et al for treating tumor metastasis is indistinguishable from a drug of the present invention as claimed for treating a heart disease.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/
Primary Examiner, Art Unit 1633